

## **REMARKS**

### Status of the Claims

Claims 1-27 are currently pending. Claims 9-26 are withdrawn from consideration as being directed to a separate invention. Claims 1-8 and 27 are currently under examination.

### Priority

As requested, Applicants have updated the first paragraph of the specification to include a reference to PCT/US2004/021646. However, Applicants respectfully point out that it is not necessary to amend the first sentence(s) of the specification to reference the international application number that was used to identify the application during international processing of the application by the international authorities prior to commencement of the national stage (see MPEP 1893.03(c)(III), page I800-207 (8th Ed.)).

### Drawings

The Office Action objected to the drawings as failing to label panels “A” and “B” for figures 7 and 8. Since the Patent Office has not issued a PTO-948 requiring Applicants to relabel the panels in figures 7 and 8 with “A” and “B,” Applicants have not corrected the drawings. However, Applicants have amended the Brief Description of figures 7 and 8 to be consistent with the figures.

### Amendments to the Specification

As requested, the specification has been amended to reference trademarked names in a proper manner.

### Abstract

As requested, an abstract on a separate sheet is attached to this paper.

### Amendments to the Claims

Claim 3 has been amended to define acronyms in their first instance. The amendment to

claim 3 does not introduce prohibited new matter.

#### Claim Objections

The Office Action objected to claim 3 for not defining acronyms in their first instance. Claim 3 has been amended to define the acronyms.

#### Rejections under 35 U.S.C. § 102(b)

A. Claims 1, 4, 7, and 8 are rejected under 35 U.S.C. § 102(b) as anticipated by Berner *et al.* (Ann. Rheum. Dis., 2000, Vol. 59, pp. 190-195).

The present invention is directed to a method of determining whether a subject has an auto-immune disease by detecting the level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in the blood of the subject. Berner *et al.* do not disclose the claimed invention. Berner *et al.* only teach detecting CD4<sup>+</sup>CD40L<sup>+</sup> which is not the same as detecting CD4<sup>lo</sup>CD40<sup>hi</sup>. Applicants respectfully point out that the specification defines CD4<sup>+</sup>CD40<sup>+</sup> as being the same as CD4<sup>lo</sup>CD40<sup>hi</sup>, but the specification does not define CD4<sup>+</sup>CD40<sup>+</sup> as being the same as CD4<sup>+</sup>CD40L<sup>+</sup>. CD40L (also known as CD154) is a ligand for CD40. Therefore, CD4<sup>+</sup>CD40<sup>+</sup> is not the same molecule as CD4<sup>+</sup>CD40L<sup>+</sup>. Accordingly, Berner *et al.* do not anticipate the present invention.

B. Claims 1, 4, 5, and 7 are rejected under 35 U.S.C. § 102(b) as anticipated by Wagner *et al.* (PNAS, March 19, 2002, Vol. 99, pp. 3782-3787).

The present invention provides a novel method of determining whether a patient has an auto-immune disease comprising detecting elevated levels of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in the blood of a subject. The Office Action alleges Wagner *et al.* anticipate the claimed invention because Wagner *et al.* disclose functional expression of CD40 on CD4<sup>+</sup> T cells in nonobese diabetic (NOD) mice. Applicants respectfully point out that Wagner *et al.* neither disclose nor suggest that an increased level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in the blood sample of a subject as compared to a control sample of blood is indicative that the subject has an auto-immune disease. Wagner *et al.* only disclose functional expression of CD40 on CD4<sup>+</sup> T cells in NOD mice. Wagner *et al.* do not disclose or suggest detecting an auto-immune disease, and Wagner *et al.* do not teach or suggest comparing the levels of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells from a subject and from a control sample

for determining whether the subject has an auto-immune disease. Moreover, Wagner *et al.* do not teach or suggest that increased levels of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells are predictive of an auto-immune disease, even in mice, but rather only teach that CD4<sup>lo</sup>CD40<sup>hi</sup> T cells are increased as a percentage of T cells in NOD mice. Accordingly, Wagner *et al.* do not anticipate the claimed invention.

Rejection under 35 U.S.C. § 103(b)

Claims 2, 3, and 6 are rejected under 35 U.S.C. § 103(b) as obvious under Berner *et al.* or Wagner *et al.* in view of Jeffery (Novartis Foundation Symposium, 2001, vol. 234, pp. 149-161, Abstract) and Waid *et al.* (FASEB, 2003, 17(7), p. C177).

Claims 2, 3, and 6 depend directly or indirectly from Claim 1 and are drawn to methods of determining whether a subject has at least one auto-immune disease. The present application does not include product claims. Applicants respectfully request clarification of this rejection. If the Examiner intended to reject the claims under 35 U.S.C. § 103(a), Applicants respectfully request that a new rejection be made in the next Office Action and that the Office Action be issued as a Non-Final Office Action.

Nevertheless, Applicants submit that the cited references do not render the claimed invention obvious. The deficiencies of Berner *et al.* and Wagner *et al.* are discussed above. Applicants respectfully submit that the teachings of Jeffery and Waid *et al.* do not cure the deficiencies of Berner *et al.* and Wagner *et al.* Jeffery only teaches a CD4/CD8 ratio may affect regulation of IL-4 and IL-5. Waid *et al.* only teach injecting OVA increases CD4<sup>+</sup>TCR<sup>+</sup>CD40<sup>+</sup>, IL-2, IL-4, IL-10, and IFN $\gamma$  levels. Neither Jeffery nor Waid *et al.* provide a method for determining if a subject has an auto-immune disease by comparing CD4<sup>lo</sup>CD40<sup>hi</sup> levels to a control. Accordingly, the combination of the cited references does not render the claimed invention obvious.

Rejection under 35 U.S.C. § 103(a)

Claim 27 is rejected under 103(a) as obvious under Berner *et al.* or Wagner *et al.* in view of Foster *et al.* (US Patent 4,444,879).

Claim 27 is directed to a kit for detecting CD4<sup>lo</sup>CD40<sup>hi</sup> T cells. Foster *et al.* do not cure

the deficiencies of Wagner *et al.* and Berner *et al.* The deficiencies of Berner *et al.* and Wagner *et al.* are discussed above. Foster *et al.* are relied upon for disclosing kits, but Foster *et al.* do not teach or suggest that an expanded level of CD4<sup>lo</sup>CD40<sup>hi</sup> T cells in the blood sample of a subject as compared to a control sample of blood is indicative that the subject has an auto-immune disease.

Accordingly, there is no motivation to combine the teachings of Berner *et al.* or Wagner *et al.* with Foster *et al.* and to make the necessary changes to obtain the kit recited in the present claim with reasonable expectation of success. Accordingly, the combination of the cited references does not render the claimed invention obvious.

#### Double Patenting

Claims 1, 4, 5, 7, 8, and 27 are provisionally rejected on the ground of obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application 10/399,384 ('384).

The Office Action alleges that the claims are directed to methods that are not patentably distinct from each other. Applicants respectfully point out that the present application is directed to a method of determining whether a subject has an autoimmune disease, while Application '384 is directed to a method of determining whether a subject has type I or type II diabetes. Diabetes is a species of the genus of autoimmune diseases. Therefore, the claimed invention of the present application are not an obvious variation of the claimed invention of Application '384.

Moreover, the present application is a national phase application of international application PCT/US04/21646, filed on July 7, 2003. Application '384 was filed on April 7, 2006, as a continuation-in-part application of the present application. The present application with claims directed to the genus has an earlier filing date than Application '384 with claims directed to the species. Accordingly, the present application does not render the claimed invention of Application '384 obvious.

The claimed inventions of the two applications are patentably distinct.

Claims 2, 3, and 6 are provisionally rejected on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 1-13 of copending Application No.

11/399,384 ('384) in view of Jeffery and Waid *et al.*

For the reasons discussed above, the claimed inventions of the present application and Application '384 are patentably distinct.

Application '384 is directed to determining whether a subject has type I or type II diabetes. Jeffery and Waid *et al.* are not directed to determining whether a subject has type I or type II diabetes. Also as discussed above, neither Jeffery nor Waid *et al.* teach a method for determining if a subject has an autoimmune disease by comparing CD4<sup>lo</sup>CD40<sup>hi</sup> levels to a control. Accordingly, there is no motivation to combine the teachings of the cited references and to obtain the claimed invention. Thus, Application '384 and the cited references do not render the claimed invention obvious.

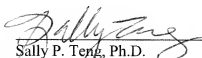
### Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, she is invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

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Respectfully submitted,  
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